

A Challenge for Toxicologists¹

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One of the most interesting periods of my life was when I was trying to double up and be a journalist as well as a scientist. I spent five or six years writing a weekly column for the *Washington Post*. In fact, I guess I was one of the early environmental writers. In the middle sixties, there was almost nothing in the press about the kinds of issues that appear today on a daily basis. I felt I was in a position to blow the whistle on lead, on chlorine, on a wide variety of other environmental additives. Mostly, I made somewhat ambiguous statements about them: namely, there was some cause for concern about the levels to which we were being exposed but that we really did not have adequate scientific information to make a conclusive assessment.

I read my columns closely enough to begin to be persuaded of the priority of scientific attention that these issues deserve. And so, one of the consequences of that involvement was my own growing conviction that the scientific analysis of environmental health was a matter that served a far higher centrality of attention within our academic circles than it had at that time—or that it enjoys at the present time.

I really have a very strong conviction about the centrality of these issues of environmental health, and I have some informed skepticism about the adequacy of our scientific knowledge in order to deal with these toxic substances at a policy level to provide reasonable optima in terms of limiting human exposures. And, of course, I am dismayed about the very nearly total irrelevance of most of the testing that goes on these days to try to reach useful conclusions about standard setting, about definitions as to what we should and should not permit by way of exposure.

I say that as against the hope that we may reach the time when we can use the more comprehensive, more nearly rational cost-benefit analysis and not say merely which compound puts us at risk of dire results. We must at a quantitative level understand within a factor of 10 or even 100 just what damage is going to be done.

Now, for the first one, ten, or hundred substances for which a campaign was

¹ Excerpted *ex tempore* remarks by Dr. Lederberg, Nobel Laureate, on *Toxic Substances and the News Media: Scientific and Value Issues*, made January 12, 1981, at The Rockefeller University to launch the World Environment Center, New York City.

developed it was perhaps acceptable to say "here are the hazards, we don't know how to measure it, let's eradicate it." But when we reach the point that a very significant part of our total chemical and total technological industry is faced with those challenges to every innovation, we obviously need to do a better job than we are doing today or we will end up in total paralysis. We will have a paralysis of innovation. We will be stuck with what we have, and what we have is not always that wonderful with respect to the levels of environmental safety.

So, I have felt very strongly that there were issues of national policy to which there was a responsibility for the development of better scientific information, and that we did not have adequate institutions to meet those responsibilities.

With all of the enormous expansion both in quality and in quantity—that is, in the variety and total material—of the chemical industry, I believe today that we're in a far healthier position than we were 30 years ago. Thirty years ago, there were fewer substances being emitted, but the abandon that they were being dealt with! You had workers walking knee deep in solvents and paying absolutely no attention to them. Since then, there has been a sharp increase in vigilance. With respect to a wide variety of substances, I am quite confident that the average exposure to many of these chemicals is down by a factor of 10 or 100 compared to what it was in the early 1950s, just on account of the awareness that has been generated—the public sensitivities about these matters. There is no major industry today that does not now have a deeply ingrained environmental apparatus—procedures, bureaucracy, and doctrine—with respect to control of environmental problems. This is an enormous advance over what was the case 30 years ago.

We have at this point, of course, the responsibility to work out procedures that will provide for appropriate surveillance of new substances, for prevention of human exposure where it really is of some consequence. This in turn presents an enormous challenge to scientific enterprise; it is just beginning to be met.

If there is any message that I would like to see conveyed it is the gross inadequacy of our present knowledge base to properly face the enormous environmental challenge that we have at the present time.

I think the testing of substances could be greatly improved, improved above all by better understanding of the mechanisms by which these substances work. Right now there is almost no rationale for deciding whether the mouse, the rat, the rabbit, the guinea pig, or the monkey is going to be the better model for effects on human behavior. In fact, very few substances have been tested using more than one species in order to build up a body of theory to project in what way the human is likely to be more or less like other animals.

For that reason, I have felt a particular priority should be given to that discipline that hardly exists today, which I would call comparative toxicology. When it comes to toxic substances the prevailing doctrine is to find the most sensitive animal and if you can get a toxic effect, there is a potential hazard in man. Therefore, under most circumstances, you need to abolish the substance if you can produce cancer in that animal. Well, I cannot argue against that in any affirmative way, with the present state of our knowledge, but it is obviously fraught with all kinds of difficulties and false positives. It is being excessively rigorous in a few cases when there are 10,000 other things that have not been looked at yet.

First of all, understand that the one or two or three hundred millions of dollars a year that we are now spending on routine animal tests are almost all worthless

from the point of view of standard setting. It may be appropriate for setting alarms, but once you obtain a bladder cancer in a certain percentage of male mice who have been through two generations of saccharin treatment, what then? Is the male mouse a good model for the male human, is that two-generation bit really a significant element, without knowing the mechanisms by which saccharin may be acting?

I would think the most immediate solution is to redeploy some of our resources. The resources are not only money; there is the time and effort. The whole quality of the field of toxicology has been so drowned by the requirement to do these kinds of tests that this, in itself, has made it a less respectable discipline from the point of view of more fundamental biological interests.

It is not justifiable to expose human beings to substances whose risk to them is not perceivable at the present time. But we do not take sufficient advantage of those unfortunate circumstances where human beings are inadvertently exposed to environmental chemicals of one kind or another. I cannot imagine any conceivable objection on the worker's part to being taken care of very well and being monitored very closely to try to see what the metabolism of benzene, for example, is like in a human being. In fact, you could have the opportunity to take some advantage of that misfortune that would be of benefit to others. We have no institutional arrangements for doing that kind of study. It is something I am particularly interested in trying to set up. It would obviously require carefully worked-out cooperation with the unions, with the companies, with the academic institutions. But at least, when those kinds of accidents happen, we can make sure they are of some sort of benefit for the future.

The point I am trying to make is that it is simply not possible with all the animals in the world to test new chemicals in the blind way that we use at the present time, and reach credible conclusions about the hazards to human health. We are at an impasse. It is one that has deep scientific roots, and we had really better do something about it.

I am delighted about the increasing role of private industry in research and development. There is a cooperative industrial venture, the Chemical Industry Institute for Toxicology, that I have thought well enough of to happily be a member of the board. I am very much impressed by this as an independent laboratory under cooperative financing. I think this is the cutting edge of exactly the kind of research that I was advocating. The larger industrial companies have got to do it in order to meet regulatory requirements, and to sensibly anticipate the future. The last thing an industry wants to discover after it has invested one hundred million dollars and set up a plant to produce something is that it has some toxic effect that will paralyze that industry further. Plainly industry not only has to meet present mandatory standards but has to be able to look ahead ten years, when that plant first comes on stream, because that is when the hard punches are going to come.

I think the main limitation for industrial performance in this area is that presently we do not have an adequate academic base for the adequately trained toxicologist to meet the jobs that industry has opened up, much less the expansion we require on the academic side as well. But industry has no choice but to invest a great deal of money in this area. It is a small fraction of what is at stake from their own standpoint with respect to further marketing of these materials.